TECHNIQUE

Intravascular ultrasound in patients with acute pulmonary embolism after treatment with intravenous urokinase and high-dose heparin

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Abstract

Objective—To compare the diagnostic value of intravascular ultrasound (IVUS) with angiography in patients with pulmonary embolism.
Design—Open, prospective clinical study.
Setting—Two university hospitals.
Patients—Angiography and IVUS were used in 11 patients (5 men) (mean (SD) age 50 (18) years) with acute pulmonary embolism.
Interventions—At a mean (SD) of 6 (4) hours after thrombolytic therapy with urokinase and full-dose heparin, all patients underwent pulmonary artery angiography. Then 3·5 F mechanical, 20 or 30 MHz IVUS catheters were advanced into the pulmonary circulation.
Main outcome measures—The pulmonary circulation was studied by both methods to detect the presence of thrombus, and a modified Miller score (assessing perfusion defects only and not velocity of flow) was used to quantify the angiographic images.
Results—The modified Miller score was mean (SD) 7·4 (2·3) points. 168 pulmonary artery segments (diameter range 2–14 mm) were studied by angiography and IVUS. On angiography, seven segments showed complete obstruction and 49 partial obstruction; 112 were normal. Two distinct types of thrombus formation were found by IVUS. Type A thrombus only partly adhered to the wall but otherwise was mobile and type B predominantly adhered to the wall. IVUS confirmed all seven angiographically complete obstructions but missed three (6%) of the 49 partial occlusions. Forty (87%) of the remaining 46 segments had type A thrombus and six (13%) type B. IVUS indicated a thrombus in 38 (34%) of the 112 angiographically normal segments; 20 (53%) showed a type A pattern and 18 (47%) a type B pattern (P < 0·001).
Conclusion—IVUS was more sensitive than angiography in detecting thrombus but the clinical impact of this finding is not clear as yet.

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In acute pulmonary embolism, rapid diagnosis and prompt and appropriate treatment are crucial to outcome.[1][2] The diagnostic approach has changed over the past two decades, mainly owing to the introduction of non-invasive tests such as ventilation-perfusion scans and echocardiography.[3] Transthoracic echocardiography enables us to determine non-invasively the pulmonary artery pressure and the right ventricular volumes and function. Transoesophageal echocardiography has the additional advantage of identifying proximal pulmonary artery embolism in some patients.[4-10] Thus patients identified as having haemodynamically relevant embolic events can be treated early with full-dose heparin and, if necessary, with thrombolytic agents.[11-14]

In patients with suspected pulmonary embolism, angiography is an invasive method that gives a rapid and complete image of the entire pulmonary circulation, yet it need not be performed in all patients. Moreover, the injection of ionic, high-osmolality contrast material puts critically ill patients at increased risk; non-ionic low-osmolality contrast agents are usually well tolerated.[15][16] However, the imaging of partially occluded vessel segments by angiography has been liable to misinterpretation.[16]

Intravascular ultrasound (IVUS) is a new technique that images the lumen and the vessel wall by means of very small ultrasound probes. It is likely to be useful in the diagnosis of abnormalities of the pulmonary circulation.[17][18] Our group was among the first to show the diagnostic value of IVUS in a patient with acute pulmonary embolism.[19] Tapson *et al* reported their initial experience with IVUS in a canine model of pulmonary embolism and in a limited number of patients, as did Ricou *et al* in patients with recurrent thromboembolic disease.[20-22] The aim of our study was to investigate further the feasibility, accuracy, and safety of IVUS in patients after thrombolytic treatment for acute pulmonary embolism, and to compare the results with angiography.

Clinical and haemodymanic measurements (obtained during angiography), and demographic data on 11 patients studied prospectively

Case	Sex	Age	BSA (m²)	HR (min⁻¹)	PA syst (mm Hg)	PA dias (mm Hg)	PA mean (mm Hg)	PCW (mm Hg)	CI (l⁻¹/m²)	Pulmonary resistance (dyn.s.cm⁻⁵)	PO² (mm Hg)	PCO² (mm Hg)	Clinical outcome
1	F	20	1·80	112	26	12	16·7	7	2·5	172	58	33	Alive
2	F	30	1·95	100	45	18	27·0	10	1·7	410	61	29	Alive
3	F	62	1·60	90	31	15	20·3	8	3·2	193	66	34	Alive
4	M	57	1·80	124	51	29	36·3	5	2·8	497	60	37	Alive
5	M	65	2·45	54	60	15	30·0	7	2·4	313	72	45	Alive
6	F	18	1·70	68	24	14	17·3	5	3·2	181	65	41	Alive
7	F	60	1·90	103	52	25	34·0	11	2·8	346	80	43	Alive
8	M	54	2·10	105	44	16	25·3	5	2·8	277	57	34	Alive
9	M	47	1·60	66	56	23	34·0	8	2·1	619	55	32	Surgery
10	F	65	1·65	102	47	18	27·7	9	1·7	532	50	48	Alive
11	M	73	1·75	88	38	16	23·3	9	2·9	226	81	29	Alive
Mean (SD)		50 (18)	1·85 (0·24)	92 (20·4)	43·09 (11·45)	18·27 (4·97)	26·55 (6·42)	7·6 (2·0)	2·6 (0·5)	342 (147)	64 (10)	37 (6)	

One patient (case 9) had recurrent thrombembolic events and underwent successful thromboendarterectomy. All patients were discharged alive and well. BSA, body surface area; PA, pulmonary artery; syst, systolic; diast, diastolic; PCW, pulmonary capillary wedge pressure; CI, cardiac index.

Patients and methods

PATIENTS

Patients with the diagnosis of acute pulmonary embolism based on clinical signs such as shortness of breath, heart rate > 100 beats/min, systolic blood pressure < 110 mm Hg, and the additional finding of right ventricular overload during echocardiography, or of a positive ventilation-perfusion scan, and who were suitable for thrombolytic therapy, were entered prospectively in our study over a 23 month period. The patients underwent right heart catheterisation and angiography of their pulmonary arteries mean (SD) 6 (4) hours after treatment with three million units of urokinase in one hour, and a bolus injection of 10 000 units of heparin, followed by continuous infusion for 48 hours. All patients were awake and gave their informed consent for the thrombolytic therapy, angiography, and the IVUS study. The use of IVUS catheters was approved by the local ethics committees and the study complied with the Declaration of Helsinki. All patients with vascular access from the legs had an angiographic study or ultrasonic examination of their femoral and pelvic veins before puncture to rule out thrombus formation.

METHODS

Angiography was performed using a Siemens HICOR, BICOR, or MICOR system. A pigtail catheter was advanced through an introducing sheath placed in a femoral or brachial vein, and selectively positioned in the right and left pulmonary arteries. Non-ionic contrast material (45–55 ml in each side, 10–14 ml/s) was injected selectively into the left and right pulmonary circulation. Pulmonary capillary wedge pressure and pressures in the pulmonary artery, right ventricle, and right atrium were measured with 7·5 F Swan-Ganz catheters.

For the IVUS study we used 3·5 F, mechanical, 20 or 30 MHz, monorail echo transducers (Boston Scientific, Waterton, MA, USA) connected to a Hewlett Packard Sonos or Diasonics echo system with S-VHS video recording.

ANALYSIS

The severity of embolisation in the pulmonary circulation was judged from the angiographic findings using the Miller score to assess embolic involvement (but not the effect on pulmonary contrast flow) as described in detail elsewhere.[11] The diameter of the pulmonary arteries was calculated from the angiograms using the pigtail catheter for calibration.

The Miller score was calculated by two physicians blinded to the results of the other colleague. The IVUS images were also analysed by two cardiologists to determine the minimal and maximal lumen diameters and the nature of thrombus formation (complete obstruction, wall adherent, or partially mobile echodense structures). The clinical course of the patients was followed until discharge from the hospital.

STATISTICAL ANALYSIS

All statistics were calculated using a commercially available and validated program (SAS, release 6·04, SAS Institute; Cary, NC, USA) for MS-DOS computers. Values are given as a mean (SD). The pulmonary artery diameter measurements by angiography and IVUS were plotted by the graphical technique proposed by Bland and Altman.[23] The presence or absence of a thrombus was compared using a chi-square table.

Results

Eleven patients were studied by both methods. The patient's characteristics, their haemodynamic variables during the invasive study, and

Figure 1   Comparison of diameter dimensions obtained by angiography and intravascular ultrasound in angiographically normal pulmonary arteries (Altman-Bland plot).[23] Standard error (SD) was 0·6 mm, and IVUS underestimated diameters larger than 5 mm in comparison with angiography. (n = 33)
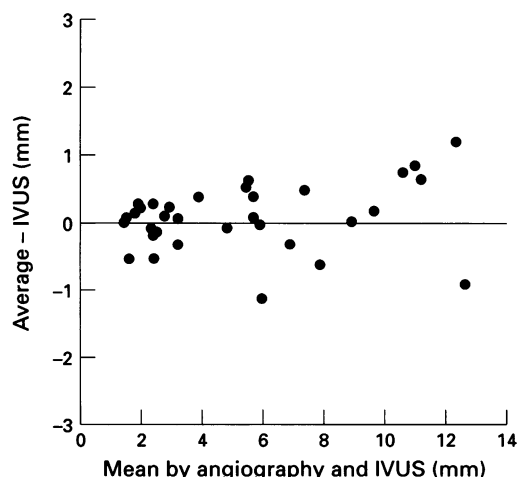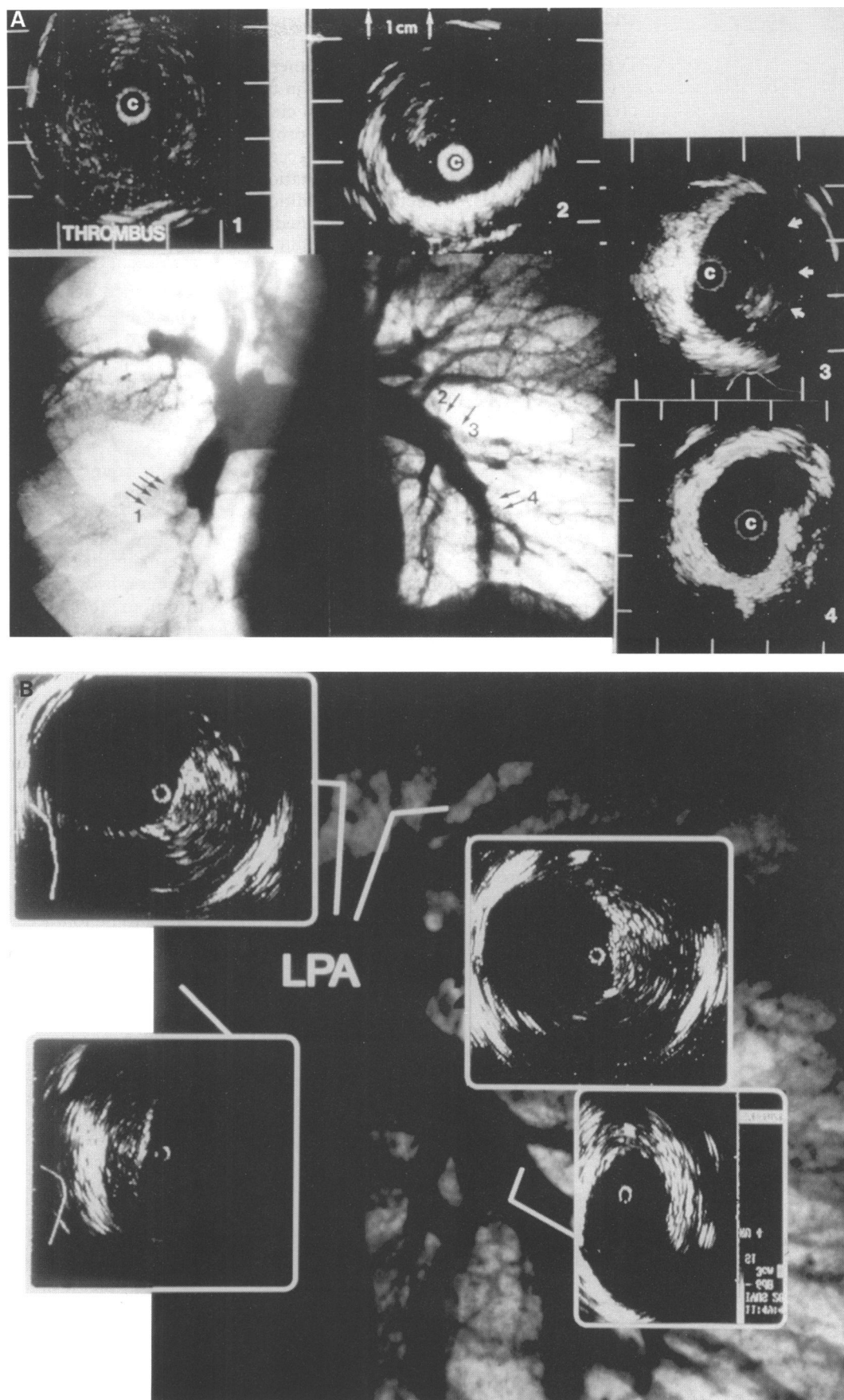
*Figure 2 (A)
Intravascular appearance
of acute pulmonary
embolism. Non-circular,
soft partly mobile thrombus
(type A pattern) in
positions 2–4. Complete
obstruction in position 1.
(B) Typical example of the
intravascular appearance
of an old, recanalised
thrombus (type B pattern,
wall adherent, non-
mobile), confirmed by
surgery.*

their clinical outcomes are summarised in the table. All patients were discharged alive and well, and there were no adverse events attributable to the thrombolytic therapy, angiography, or IVUS examination.

The Miller index ranged from 4 to12 points

(mean (SD) 7·4 (2·3)). A total of 168 pulmonary artery segments were studied by both methods. On the basis of the angiographic results, seven segments showed complete obstruction, 49 partial obstruction and angiographic signs typical of thrombus formation,

and 112 segments were normal. There was good agreement between angiography and IVUS measurements of luminal diameter in vessels ranging from 3 mm to 14 mm in diameter (fig 1). In nine of 11 patients no circumferential image was obtained in the proximal pulmonary arteries because of the eccentric position and limited far-field penetration of the 20 or 30 MHz catheters. In addition to complete obstruction, IVUS identified two additional types of thrombus formation. The first type (type A) was thrombus partially adherent to the vessel wall, but otherwise mobile (fig 2A). The second type was thrombus completely adherent to the vessel wall, either circumferential or in a half moon shape (type B) (fig 2B).

Though the correlation between IVUS and angiography was 100% in seven segments with complete obstructions, there were differences both in angiographically normal and partially occluded vessel segments. Three (6%) of the 49 angiographically partially occluded vessel segments showed no signs of thrombus formation during IVUS; probably because the IVUS examination was performed after angiography and the thrombus may have resolved. Forty (87%) of the remaining 46 segments showed type A thrombus during IVUS and six (13%) showed a type B appearance.

IVUS revealed thrombus in 38 (34%) of the 112 angiographically normal segments. Twenty (53%) showed a type A pattern and 18 (47%) a type B pattern (P < 0·001).

In general, IVUS had a higher sensitivity for thrombus formation than angiography, mainly for wall adherent but also for partially wall adherent and mobile thrombi. Of the 38 segments with thrombus confirmed by IVUS but negative angiographically, 14 were found in the proximal pulmonary artery, 15 in a first level branch, and nine in a second level branch.

The additional fluoroscopy time for the IVUS study was 3·75 (0·8) minutes (range 2–7·5 minutes). No IVUS related complications occurred. All patients were discharged alive and well. In one patient, recurrent pulmonary embolic events with persistent pulmonary hypertension was diagnosed. He underwent successful thromboendarterectomy later.

Discussion

The present paper describes the experience with both angiography and IVUS in patients with acute pulmonary embolism after thrombolytic therapy. The main finding was that IVUS revealed thrombus formation in 38% of angiographically normal segments. Furthermore, two different types of pulmonary thrombus formation could be identified: type A, a partially wall adherent, but otherwise mobile thrombus; and type B, a thrombus most of which is attached to the vessel wall. In addition, thrombus formation was found in the inferior vena cava in two patients in whom it was not detected by other techniques. Our findings concerning the feasibility and safety of

IVUS in patients with pulmonary hypertension accord with the findings of Ricou *et al* in patients with recurrent thromboembolic disease and with the initial experiences of Tapson *et al* and Scott *et al*.[20–22][24]

PRESENT LIMITATIONS

The IVUS catheters presently available are designed for use in the coronary arteries and are not steerable. Because of limited steerability they were often in eccentric position, with the consequence that the diameters could not be determined accurately in all segments of the pulmonary circulation. The first experience with a new steerable IVUS catheter showed that this design may overcome this limitation, as may the forward viewing crystals.[25][26]

Although the sensitivity of IVUS for the detection of thrombus was superior to that of angiography, even high frequency intravascular ultrasound may miss very fresh thrombus formation.

CLINICAL IMPLICATIONS

The main diagnostic advantage of IVUS over angiography was that it revealed more residual thrombus formation. However, the clinical implication of this finding is unclear and in the present study the IVUS findings did not affect the clinical consequences. IVUS has already been shown to be superior to angiography in the coronary circulation. Angiography is a contour method and thus limited to imaging the contrast-filled lumen.[27] It may therefore overlook recanalised or predominantly wall adherent thrombus with a regular surface. The haemodynamic significance of residual, angiographically overlooked thrombi and their clinical implication are as yet not known, nonetheless in theory IVUS may allow such lesions to be followed up.

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